Heart Transplantation

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Disclosure statement

• There are no Conflicts of Interest to disclose
CRISIS AFTER 7 DAYS

Louw tells of key factor in heart transplant

Woman had no chance of survival

Head of team

And a surgeon took the pictures, too!

Churchmen approve

Man with a new heart

Three years' work on 'op'

They will miss Denise...

Look Ma! No Pins

From a word of the editor of The Cape Argus in defence of British democracy.

Grooto Schuur doctors say
Christiaan N. Barnard
Adult and Pediatric Heart Transplants

Number of Transplants by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>1982</td>
<td>187</td>
</tr>
<tr>
<td>1983</td>
<td>322</td>
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<tr>
<td>1984</td>
<td>571</td>
</tr>
<tr>
<td>1985</td>
<td>1,261</td>
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<td>1986</td>
<td>2,358</td>
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<td>2,997</td>
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<tr>
<td>1988</td>
<td>3,526</td>
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<tr>
<td>1989</td>
<td>3,873</td>
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<tr>
<td>1990</td>
<td>4,524</td>
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<tr>
<td>1991</td>
<td>4,747</td>
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<td>1992</td>
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<td>1993</td>
<td>4,921</td>
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<td>1994</td>
<td>4,821</td>
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<td>1995</td>
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<td>1996</td>
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<td>2008</td>
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<tr>
<td>2009</td>
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<tr>
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<tr>
<td>2011</td>
<td>4,921</td>
</tr>
<tr>
<td>2012</td>
<td>4,921</td>
</tr>
</tbody>
</table>

NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide.
Indications

- Congestive heart failure, New York Heart Association (NYHA) Class III or IV symptoms, with objective evidence of impaired functional capacity (peak oxygen consumption <14 mL/kg/min), despite optimal medical therapy
- Refractory angina, despite maximal medical therapy, and not amenable to revascularization
- Refractory life-threatening ventricular arrhythmias, despite maximal antiarrhythmic therapy
- Congenital heart disease with progressive ventricular failure that is not amenable to conventional surgical repair
- Severe hypertrophic or restrictive cardiomyopathy
Contraindications

1) Mean transpulmonary gradient >15 mmHg, and/or peripheral vascular resistance >5 Wood units on maximal vasodilator therapy
2) Active infection (unless associated with left ventricular assist device)
3) Irreversible extra-cardiac organ disease (liver, kidney, ...)
4) Morbid obesity (body mass index >35 kg/m²)
5) Severe diabetes mellitus, with end-organ damage
6) “Severe peripheral vascular disease”
7) Recent stroke (unless associated with left ventricular assist device)
8) Acute pulmonary embolism (<6 wk)
9) Active neoplasm
10) Severe psychiatric or cognitive impairment, non-compliance, lack of family or social support
Adult Heart Transplants Diagnosis

For some retransplants diagnosis other than retransplant was reported, so the total percentage of retransplants may be greater.
Donor Allocation and Selection

• Priority system based on severity, distance, time on list, size and ABO blood type
• 3 Tier system
  – 1A, 1B, 2
Donor Guidelines

- Age < 55 years
- HIV/HBV negative
- No severe infection
- No extracran malign
- No severe card trauma
- No severe CAD
- Accept ventr function
- Dopa < 10 ug/kg/min
- Blood type compatib
- Body weight 80-120%
- Neg prosp Xmatch
- Ischemic time < 4-5 h

Costanzo MR et al. J Heart Lung Transplant 2010;29:914
Adult and Pediatric Heart Transplants
Donor Age by Year of Transplant

% of transplants

0-9 10-17 18-39 40-59 60-69 70+
Median Age

2014 ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
JHLT. 2014 Oct; 33(10): 996-1008
Risk Factors For 1 Year Mortality with 95% Confidence Limits

Donor Age

Hazard Ratio of 1 Year Mortality

Donor Age (years)

p < 0.0001

(N = 10,739)
Interaction between donor age and the ischemic time of the 5-year mortality risk after heart transplantation.

Surgical Technique

- Biatrial technique - Lower and Shumway 1960
- Bicaval technique - Sievers 1991
  - Less disruption of atrial anatomy
  - Better RV function
  - Less MV and TV regurgitation
  - Less sinus node dysfunction
Peri-operative Management

- Left atrial line
- CVP monitoring
- Nitric Oxide
- Continued inotropic support for 72 hours
Immunosuppressive Regimen

- Induction therapy (Renal insufficiency)
- Calcineurin Inhibitors (Tacrolimus)
- Anti-metabolites (Mycophenolate Mofetil)
- Steroid
Adult Heart Transplants
Induction Immunosuppression by Transplant Type
(Transplants: January 2005 – June 2013)

Analysis is limited to patients who were alive at the time of the discharge.
Adult Heart Transplants
Kaplan-Meier Survival by Induction Type
Conditional on Survival to 14 Days
(Transplants: January 2001 – June 2012)

No induction vs. IL-2R: p = 0.0098
IL-2R vs. Polyclonal: p = 0.0179
No other pair-wise comparisons were significant at p < 0.05.
Postoperative Management

- Prevent rejection
  - Prednisone
  - Cyclosporine/tacrolimus
  - AZA/MMF/sirolimus

- Allograft vasculopathy
  - Aspirin
  - Pravastatin
  - Vitamin C, E

- Prophylaxis
  - Bactrim (PCP, Toxo)
  - Valcyte (CMV)
  - Mycelex (Thrush)

- Hypertension
  - Avoid beta-blockers

- Diabetes

- Frequent clinic visits
  - Twice weekly for the first month
  - Once weekly for month 2
  - Month 3, 4, 5, and 6
  - Month 8, 10, 12
  - Every 3-6 months for life

- Assess for rejection
  - History and physical
  - Echocardiogram
  - Endomyocardial biopsy
    - 13-16 in the first year
    - No routine bx after first year

- Assess for TCAD
  - LHC +/- IVUS at 6 wks and annually
Classification of Rejection

• Signs and symptoms
  – Atrial Fibrillation/Atrial Flutter
  – CHF signs and symptoms
  – Systolic dysfunction/Echocardiogram

• Cellular rejection: leukocytes and necrosis
  – Grade 0: no rejection
  – Grade 1R: mild rejection
  – Grade 2R: moderate rejection
  – Grade 3R: severe rejection

• Humoral rejection
  – Antibody-mediated
  – Capillary swelling, macrophages, Immunoglobulin and complement deposits
## Treatment of Rejection

<table>
<thead>
<tr>
<th>Cellular</th>
<th>Reduced EF</th>
<th>Heart Failure/Shock</th>
</tr>
</thead>
</table>
| • Target higher CNI levels  
• Oral steroid bolus + taper  
• Rapamune | • Oral steroid bolus/taper  
or  
• IV pulse steroids | • IV pulse steroids  
• Cytolytic therapy (ATG)  
• Plasmapheresis  
• IV immune globulin  
• RHC/Inotropic therapy  
• IABP or ECMO support |
| Humoral | • Oral steroid bolus/taper  
or  
• IV pulse steroids  
+/-  
• IV immune globulin  
• Plasmapheresis, velcade | No treatment? |
**UCLA HTx Surveillance Protocol 7/1/11**

* Single-antigen-based antibody testing (or flow crossmatch) in suspected rejection/graft dysfunction (frequency determined by clinical suspicion)

** Bx including C4D/CD68 (do also single-antigen-based antibody testing & cylex)

*** Allomap (do also single-antigen-based antibody testing & cylex)

**** Earliest timepoint 2 mo (day 56) post transplant if clinician & patient feel comfortable, Echo preferentially included

***** If LOW REJECTION RISK, if HI REJECTION RISK Bx until stabilization, if INTERMEDIATE RISK> alternate Bx and ALLOMAP

****** DSE/radiouclide and LHC/IVUS alternating years if no CAV and clinician & patient comfortable
UCLA Htx 1 year Survival

Log rank
p = 0.931
Adult and Pediatric Heart Transplants
Kaplan-Meier Survival
(Transplants: January 1982 – June 2012)

Median survival = 11 years
Median survival conditional on surviving 1st year = 14 years

N = 108,343
N at risk at 27 years = 108

Survival (%) vs. Years

2014
JHLT. 2014 Oct; 33(10): 996-1008
ADULT HEART TRANSPLANTS (2007-6/2012)
Risk Factors For 1 Year Mortality

Risk factor | Hazard ratio | LCL | UCL | pvalue | N
--- | --- | --- | --- | --- | ---
Not hospitalized just prior to transplant | 0.80 | 0.70 | 0.91 | <0.0010 | 5914
Diagnosis: coronary artery disease vs. CM | 1.17 | 1.02 | 1.34 | 0.0278 | 4206
Recipient with infection req. IV drug therapy | 1.24 | 1.04 | 1.47 | 0.0162 | 1093
Transplant year: 2008 vs. 2011/2012 | 1.26 | 1.05 | 1.51 | 0.0136 | 1829
Recipient/F donor vs. M recipient/M donor | 1.27 | 1.08 | 1.50 | 0.0039 | 1598
Previous transfusion | 1.27 | 1.10 | 1.47 | 0.0010 | 2476
Transplant year: 2007 vs. 2011/2012 | 1.28 | 1.07 | 1.53 | 0.0081 | 1911
Chronic continuous flow LVAD | 1.44 | 1.21 | 1.73 | <0.0001 | 2351
Previous transplant | 1.57 | 1.19 | 2.08 | 0.0016 | 336
Diagnosis: congenital vs. CM | 1.66 | 1.18 | 2.32 | 0.0034 | 276
Total artificial heart | 1.77 | 1.14 | 2.74 | 0.0104 | 113
Recipient history of dialysis | 1.90 | 1.49 | 2.44 | <0.0001 | 278
Chronic pulsatile flow BiVAD | 1.99 | 1.45 | 2.73 | <0.0001 | 254
Ventilator | 2.03 | 1.59 | 2.61 | <0.0001 | 322
Temporary circulatory support* | 2.31 | 1.70 | 3.15 | <0.0001 | 173
RVAD | 3.26 | 1.60 | 6.65 | 0.0012 | 22

N = 10,739

* Temporary circulatory support includes ECMO and temporary pulsatile flow devices.
Complications after Heart Transplantation
## Adult Heart Transplants

Cumulative Morbidity Rates in **Survivors** within 1, 5 and 10 Years Post Transplant (Follow-ups: January 1995 – June 2013)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Within 1 Year</th>
<th>Total N with known response</th>
<th>Within 5 Years</th>
<th>Total N with known response</th>
<th>Within 10 Years</th>
<th>Total N with known response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension*</td>
<td>71.8%</td>
<td>(N = 28,163)</td>
<td>91.7%</td>
<td>(N = 13,023)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Renal Dysfunction</td>
<td>25.8%</td>
<td>(N = 31,118)</td>
<td>51.7%</td>
<td>(N = 15,769)</td>
<td>68.1%</td>
<td>(N = 5,428)</td>
</tr>
<tr>
<td>Abnormal Creatinine ≤ 2.5 mg/dl</td>
<td>17.7%</td>
<td></td>
<td>33.1%</td>
<td></td>
<td>38.5%</td>
<td></td>
</tr>
<tr>
<td>Creatinine &gt; 2.5 mg/dl</td>
<td>6.3%</td>
<td></td>
<td>14.6%</td>
<td></td>
<td>20.0%</td>
<td></td>
</tr>
<tr>
<td>Chronic Dialysis</td>
<td>1.5%</td>
<td></td>
<td>2.9%</td>
<td></td>
<td>6.0%</td>
<td></td>
</tr>
<tr>
<td>Renal Transplant</td>
<td>0.3%</td>
<td></td>
<td>1.1%</td>
<td></td>
<td>3.6%</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia*</td>
<td>59.8%</td>
<td>(N = 29,413)</td>
<td>87.6%</td>
<td>(N = 14,372)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Diabetes*</td>
<td>24.8%</td>
<td>(N = 31,120)</td>
<td>37.5%</td>
<td>(N = 15,458)</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Cardiac Allograft Vasculopathy</td>
<td>7.8%</td>
<td>(N = 28,259)</td>
<td>30.1%</td>
<td>(N = 11,511)</td>
<td>49.7%</td>
<td>(N = 3,146)</td>
</tr>
</tbody>
</table>

* Data are not available 10 years post transplant
Cardiac Allograft Vasculopathy

- 50% at 5 years
- Diffuse intimal lesions along the entire vessel wall, distinct from native vessel disease
- Diagnosis: Annual angiogram, IVUS (>0.5 mm)
- Management:
  - Risk factor management: HTN, elevated lipids,
  - Proliferation signal inhibitors
  - Statin therapy
  - Anti-platelet agents
  - PCI vs. retransplantation (timing)
Adult Heart Transplants
Survival After Report of CAV Within 3 Years of Transplant and Survival In Patients Without CAV* by Transplant Type
(Transplants: April 1994 – June 2012)

No pair-wise comparisons were significant at p < 0.05 except Primary/No CAV vs. Primary/CAV, Primary/No CAV vs. Retx/CAV and Primary/CAV vs. Retx/No CAV.

* Patient survival for those without CAV within 3 years after transplant was conditioned on survival to median time of CAV development (514 days). Median time to CAV development is based on patients who developed CAV within 3 years of transplant.
Malignancies after Heart Transplantation

- A common cause of death after the first year
- Post-transplant lymph-proliferative disorder and skin cancers
- Risk factors for PTLD: EB+ donor, intense immunosuppression, younger patients
- Treatment: Reduction of immunosuppressants and addition of proliferation signal inhibitors
No pair-wise comparisons between different transplant types within each malignancy type were significant at p < 0.05.
Frontiers of Heart Transplantation

- Donor hearts: improved utilization, ex-vivo Heart perfusion, EXPAND trial
- Improvements in immunosuppression: personalized therapies
- Non-invasive immune monitoring
- Tolerance